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THE COMPARISON OF MONOTHERAPIES OF KELOID SCARS BY LASER, SILICONE GEL, 5-FLUOROURACIL AND CRYOTHERAPY TREATMENTS - A LITERATURE REVIEW

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ABSTRACT

Keloid scars are a common problem of abnormal wound healing. There are plenty of treatment options. There is why, in this review 4 of them (laser, silicone gel, 5-fluorouracil and cryotherapy) were examined separately as monotherapies and compared.

The aim of the review was to find out whether there could be found an effective monotherapy of keloids and which one of the examined ones could be the most promising one.

In the review there were 28 studies analyzed focused on laser, silicone gel, 5-fluorouracil and intralesional cryotherapy as monotherapies of keloids.. They included some randomized controlled trials, systematic reviews, observational studies and in vitro investigations. All the literature based on combined therapies was excluded. The effectiveness, safety and rate of recurrence was assessed.

All of the therapies showed some improvements in the appearance of scars and the symptoms. However, the quality of evidence was low due to limitations of the studies and lack of long-term outcomes. Intralesional cryotherapy seems to bring the most promising results but equally the highest risk of side effects. The other 3 methods had very similar results.

None of the proposed treatments can be defined as an effective monotherapy of keloid scars. There is a high need of conducting more research focused on standardized procedures with big randomized groups of patients and the follow-ups to examine long-term recurrence rate. It could be also suggested that monotherapy may not be the best way of treatment and the further research should be focused on combined therapies.

KEYWORDS

Keloid Scars, Laser Treatment, Silicone Gel, 5-Fluorouracil, Cryotherapy, Monotherapy

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Introduction

Keloid (keloid scar, hypertrophic scar) is an extra scar grown tissue resulting from abnormal wound healing. It may occur after an injury, trauma, surgery, burns, infections or piercing. The parts of the body likely to cause keloid scars to occur are chest, back, shoulders, posterior neck and ear lobes. The process of treatment may be one of the most challenging problems in the topic of wound healing. It is also important that they do not regress spontaneously. The factors that may be prone to keloid forming may be young age, black skin, Asian or Hispanics roots or genetic factors. Keloid is not a life threatening or harmful condition and does not have to be treated. Nonetheless, patients may be concerned of itching, overgrown skin or some psychological impact and look for medical treatment. The most common ways to reduce the size of keloid are surgical removal, cryotherapy, corticosteroid injections, laser treatments, radiotherapy, 5-fluorouracyl injections, pressure therapy silicone gel or patches. Usually the actions taken are beneficial. However, very often, especially after surgical removal, the keloid scars have a tendency to recur, sometimes even larger or thicker. The rate is estimated even as approximately 80 to 100% after single surgical excision. It is very important to use appropriate care and protection of the overgrown scar. It is highly recommended to cover the keloid during sun exposure by patches or adhesive bandages and use proper sunblock protection. It is important to underline that keloids may be resistant to treatment. That is why the different methods are investigated to find the most standardized and effective therapy of treatment. Although, the problem of finding medical results may be unclear pathogenesis of keloid formation. There are some findings about higher production of collagen and additionally lower levels of degeneracy processes of collagen during the wound healing process. The only confirmed fact is that they are occurring as a result of an abnormal wound-healing process and the lack of control of regeneration and repair process mechanisms. Additionally, there is some research about the impact of inflammatory mediators such as transforming growth factor beta. Nonetheless, the pathophysiology

knowledge is still limited and needs to be explored. Due to that, there are plenty of therapies to be chosen when treating keloid scars. The medical literature does not explicitly state any standardized guidelines or protocols of keloid treatments. In our review, we decided to explore the usage of laser, silicone gel, 5-fluorouracil and cryotherapy treatments as monotherapies. Those 4 ways of treatment will be examined and compared.

The aim of this review is to find out which therapy of 4 proposed ways of treatment may result in being the most effective and simultaneously noninvasive way of treatment of keloid scars as monotherapy.

Materials and methods

Laser treatment

The keloid scars treatment by laser therapy has very limited evidence and has low to even very low certainty (R et al., 2022). The researchers studied various lasers such as pulsed dye, CO₂, NAFL and Nd:YAG. However the methodology was weak and the randomized trials were small, which makes their results inconsistent. It sums up that high-quality, well-designed clinical trials are needed before firm conclusions can be made. What is more, the side effects of lasers have to be taken into consideration. The reactions that were reported may be damage to the skin or underlying blood vessels, redness or numbness.

A research made on 16 adult patients with hypertrophic or keloidal median sternotomy scars (Alster & Williams, 1995). They used a SPTL-1 flashlamp-pumped pulsed dye laser at a wavelength of 585 nm, a pulse duration of 450 Ls, a spot size of 5 mm, and with fluence per pulse of between 6-5 and 7-25 J/cm² (mean 7-0 J/cm²). The patients received two treatments to one half of their previously untreated scars every 6-8 weeks and were reviewed at 6 months. The results show a clinical improvement in scar appearance, including reductions in redness, thickness, and symptoms such as pruritus which persisted for at least 6 months. However, the limitations of the study involved a small group of patients and very short follow-up time. To fully show the advantages of laser therapy, research should be conducted on a bigger and probably wider group of patients with different hypertrophic scars. What is more, the persistence of the results should be researched in the long term for example 5 years.

A meta-analysis of the role of laser therapy in the prevention and treatment of pathologic excessive scars, including keloids and hypertrophic scars (Jin et al., 2013). In total 919 patients were included in the research. It was reported that different laser types such as pulsed dye lasers, fractional lasers or ablative lasers may prompt scar remodeling and improve the colour, thickness and texture of the scars after an interval of 5 to 6 weeks. However, the results emphasized that laser treatment varies by laser type, timing and scar characteristics. It is needed to create standardized protocols and larger controlled studies to define long-term benefits and distinguish results by types of scars such as hypertrophic or keloid scars, because of the low level of evidence for laser therapy as a keloid treatment. It is also needed to perform research on groups of patients with different Fitzpatrick skin types because of suggestions of better results on the light skin tones.

Another investigated study involved 21 patients with hypertrophic scars (9) and keloids (12) with different etiology and body localisation (Li et al., 2020). Patients were treated with one to three treatment sessions of intralesional 1470-nm bare-fibre diode laser. Overall they observed the improvement of 42% in the HS and 37.9% in the Keloid subgroup. Additionally, no adverse side effects were reported. They described the laser technique as effective, safe and well tolerated. However, the group of patients was very small, there were no follow up studies and no long-term effects. Additionally the keloid healing was not sufficiently effective. Researchers are looking for more efficient ways of treatment.

The study of usage of combined 595-nm pulsed dye laser (PDL) and intralesional triamcinolone acetonide injection (IL TAC) compared to IL TAC monotherapy for treating HTS and keloids on 25 transgender men after bilateral symmetric postmastectomy surgeries in 4 months sessions (Rutnin et al., 2025). The study includes follow-up research after 1, 3 and 6 months after finishing treatment. The results showed significant improvement of scars appearance after 2 treatment sessions. What is more, the effect seemed to be longlasting in the follow-up study. Additionally, participants reported high satisfaction with the combined therapy and did not report any serious adverse events. There is also one more important limitation of the study, which is usage of testosterone during the laser treatment due to their gender-affirming therapy. It should be researched by some control group, whether the hormone could have any positive or negative impact on the keloid healing process.. Nonetheless, it can be concluded that usage of this laser may be helpful in treating keloid scars. However, it is highly recommended to perform a similar study on a wider group of patients to verify the results on different etiology or location of the scars. It would be also helpful to check the keloids' appearance after a few years after the treatment.

One more study of laser treatment was conducted on a group of 21 patients with dark skin colour (5 men and 16 women) in average age 30.5, who presented keloids of earlobe or helix (Piccolo et al., 2023). They represented a group with a higher risk of keloid formation. The CO₂ laser therapy was used in a single session and immediately followed by a pulse Dye laser procedure. The results were assessed after 6 months after finisher therapy by the way of dermatoscopy. It showed complete remission of keloids in the majority of patients and significant clinical improvement in keloids' size, thickness and texture. That is why it was concluded that the therapy protocol was effective and well tolerated. However, the study remains limited due to small and specific groups of patients and focused on particular areas of the body. The long-term effects were also not investigated properly and potential recurrence of keloids.

Silicone gel treatment

A systematic review based on 13 randomised controlled trials of the effectiveness of silicone gel sheeting for the treatment of hypertrophic scars included groups of patients from 10 to 60 participants (Jiang et al., 2021). Additionally, the duration of the studies and the follow-ups were different. The results showed that this type of treatment may improve the thickness, redness and overall appearance of the scars compared with no treatment. However, it was also concluded that the certainty of the evidence is rather low to even very low. None of the included studies provided clear medical evidence whether the silicone treatment is effective. What is more, it is not clearly distinguished if the effects concern keloids or only hypertrophic scars. In conclusion, silicone gel sheeting can be commonly used as a non-invasive option. However, the evidence of effectiveness is limited. It is needed to confirm more randomized controlled studies and research on some long-term benefits.

The other study of using Silgel STC-SE for the treatment of hypertrophic and keloid scars included a group of 36 patients (S. A. Stewart et al., 2016). The method was a regular application of the gel on the scars twice a day for 16 weeks. The improvement was observed after 4 and 16 weeks. The results include reductions in thickness, redness, and symptoms such as itching and discomfort. The treatment was well tolerated, with no significant adverse effects reported. It can be summarized that silicone gel is an effective and safe noninvasive option for keloid scar treatment. However, the research cannot be relevant because of a small group of patients. The study should be followed up to create some long term results. Additionally some of the observed results were not statistically significant.

A clinical trial using silicone gel sheets in a group of patients who developed keloid scars after median sternotomy indicates that regular use of silicone gel sheets can reduce some symptoms in keloid scars such as pain, itching, and redness (Sakuraba et al., 2010). What is more, it can also stabilize or even reduce progression of keloids. It is important that the therapy program was well tolerated by the patients and did not bring any serious side effects. However, the authors examined only 9 people with keloid scars. It is highly recommended to conduct a similar study with a larger randomised group of patients. It is also important to underline that some of the patients in the study used some other therapies of keloid scars before the clinical trial. It should be considered which of the interventions brought the improvement. Additionally the investigated keloids concern a very specific type of scar after the median sternotomy. The next study should focus on different locations of the human body. Nonetheless, the conclusion showed that silicone gel sheets can be used as safe, noninvasive adjunct therapy of keloid scars.

The clinical experience of using silicone gel sheeting in the treatment of keloid scars and hypertrophic scars confirmed that consistent usage of silicone gel sheets result in reduction of thickness and redness of the scars (Gold, 1993). It was also observed that the level of itching and discomfort declined in many patients. The treatment was summed up as noninvasive, well tolerated, with minimal adverse effects and easy to use. The conclusions show the usage of silicone gel sheeting in keloids treatment as a safe and effective therapeutic option. However, the study did not have any control group and the researched group of patients was very small. The follow-up was also not conducted and the long-term effectiveness was not investigated. That leads to consideration whether the silicone gel is effective in the time of use or in a longer period.

Another clinical trial of using silicone cream occlusive dressing in treatment of keloid scars showed that the therapy may lead to softening and flattening of keloids, reduction in redness, pain and itching (Wong et al., 1996). Many lesions showed partial regression or stabilization without further growth. Many of these beneficial effects were statistically significant. The therapy was well tolerated and had no serious adverse effects. The authors consider that silicone cream occlusive therapy is safe, simple and effective non-invasive treatment of keloid scars. Nonetheless, in this trial there were only 15 patients and 2 of them are children, which may influence the research results. One more time, the long-time effects were not investigated.

Using silicone gel sheets in treatment of hypertrophic and keloid disease revealed that consistent use of silicone gel sheets lead to flattening the scars, reduction of itching and redness (Eishi et al., 2003). The treatment was well-tolerated. During the trial, researchers examined the number of mast cells and Fas antigen expression. Unfortunately, the research trial was very small, they observed only 6 persons during 24 weeks. The conclusion was that this therapy is a good option for keloid and hypertrophic scars, mostly reducing pain and pruritus while improving clinical appearance. The follow-up was not conducted.

The review of effectiveness of silicone gel sheeting for the prevention and treatment of hypertrophic and keloid scars on 873 participants confirm that the results may be promising (O'Brien & Jones, 2013). The conclusions said that compared to no treatment or placebo, silicone gel sheeting may reduce the thickness, redness and general appearance of the scars. However the evidence had a very high risk of bias. Additionally, the groups sizes were small, the studies design were limited and reporting of the outcomes were inconsistent. The researchers also investigated the problem of prevention which is not a problem of this research. Additionally, some researchers in the studies mixed the definitions of hypertrophic scars and keloid scars. Due to that, it cannot be compared and varified. It can be summed up that silicone gel treatment is a noninvasive option that may reduce the keloid scars. However, it is still not fully medically confirmed.

The systematic review of 6 randomised or quasi-randomised controlled trials including approximately 300 patients showed treating specifically keloid scars by silicone gel sheeting (Tian et al., 2023). One more time, the efficiency of reducing thickness, improving colour and general appearance was confirmed. Also one more time the certainty of the evidence was low to very low. The limitations of included studies were similar as previously. It can be listed small groups of patients, limitations of methodology or risk of bias in the results. However the researchers underlined that even if the effectiveness was confirmed. The evidence is insufficient. Again there is a need to confirm more randomized controlled trials and the follow-up to check the long-term effectiveness.

Another clinical experiment with the use of silicon gel in treatment of different kinds of scars included 30 patients with scars (Puri & Talwar, 2009). The examination showed an improvement in the appearance of scars. Unfortunately, in this clinical report there were only 3 keloid scars. Additionally, the results do not clearly inform about the reduction of the keloids. It is only sad that the scars were reduced but not classified into which grade.

A metaanalyse about using silicone gel in treatment of scars included 18 high quality articles (De Decker et al., 2022). This study showed that silicone gel may help in the treatment of scars. The authors focused on hypertrophic scars and they did not mention keloid scars. However, this metaanalyse provides high quality data about the effectiveness of silicone gel. Nonetheless, it does not bring any conclusions into treating keloids.

A review in which the researchers examined the biologic mechanisms, clinical efficacy, and safety of silicone elastomer sheeting in the treatment and management of hypertrophic and keloid scars described the processes of hydrating the stratum corneum, reducing transepidermal water loss, modulating fibroblast activity and decreasing collagen deposition (Berman et al., 2007). Both the result and limitations were very similar to previous studies. The silicone gel may be helpful in scars treatment but it still needs further investigation. In keloid scars the authors showed that the treatment is limited and low-quality evidence. Nonetheless, they suggested using it as combined therapy with other methods.

5-Fluorouracil

A randomized double-blind controlled trial compared treatment of keloid by 5-FU and TAC injections included 43 adult patients with 50 keloid scars (Hietanen et al., 2019). The patients were randomly assigned to research groups. The results demonstrated the clinical effectiveness of 5-FU in some groups of patients. Additionally, 5-FU resulted in a statistically lower rate of side effects ($p < 0.05$). Unfortunately, compared to TAC, the remission rate was lower. These results were statistically insignificant. The authors suggest that 5-FU can be useful as therapy of keloids for cosmetically sensitive skin areas. What is important, The 6-months follow up examination was conducted which resulted in no statistically significant difference in remission rated between 2 research groups.

A clinical examination with usage of intralesional 5-fluorouracil as one of the methods of treatment of keloid scars had a group of 28 people (children included) (Nanda & Reddy, 2004). The therapy was conducted at weekly intervals for 12 weeks. The patients received the intralesional injections of 5-FU. The results were promising. Every keloid scar showed no failure to therapy. The results were assessed according to the size, consistency and symptoms of the scars. Additionally, none of hematological side effects was noted during therapy and it was generally well tolerated. In 24-weeks of follow-up examination there were no recurrences. The regression was noted in every patient and the satisfaction from treatment was very high. What is more, a

few patients were reported with fully flattened scars after the treatment. Unfortunately, the authors examined only 28 patients and the study was uncontrolled.

In another study there were examined 20 people with keloid scars treated with intralesional 5-fluorouracil (Kontochristopoulos et al., 2005). The observation was relatively long (1 year). Most keloids (19/20) responded at 5-FU and showed reduction of volume. One patient showed even total reduction of his scar. Unfortunately, after 1 to 6 months, 9 patients presented the recurrence after previous improvement. There were a few side effects like superficial ulceration or hyperpigmentation. Every patient reported pain after the injection, for some patients the effect was even intolerable. During examination, the authors made a histopathological examination that showed regression of histopathological changes after treatment. The authors concluded that this therapy can lead to clinical improvement of keloid scars confirmed histopathologically.

The in vitro study about the mechanism of 5-FU on fibroblasts in human keloid tissue revealed that 5-FU leads to cell cycle arrest at the G2 phase and promotes apoptosis which results in inhibited fibroblast proliferation (Huang et al., 2010). The authors emphasized also the usage of lower doses of 5-fu which led to inhibition of proliferation and cell apoptosis in varying degrees. Higher doses led to immediate apoptosis. It was summarised that using lower doses reduces risk of further scarring because of no tissue necrosis. The study creates important medical evidence from a biological perspective. It confirms that 5-FU may be an antifibroblastic therapy in keloid scars treatment. However, the study should be evidenced by some research on randomized groups of patients.

A series of cases of keloid treatment by 5-fluorouracil injections was also examined (Fitzpatrick, 1999). Unfortunately, they used 5-FU combined with other methods like steroids, Co2-laser or surgical excision. The treatment was satisfying and well tolerated. The symptoms of keloids such as thickness, redness, pain or pruritus were reduced. However, due to the non-standardized procedure of the study, the results cannot be relevant and comparable.

Cryotherapy

A study of using intralesional cryotherapy for keloid and hypertrophic scars on 10 patients (12 scars) in age range 3-54 was investigated (Har-Shai et al., 2003). The procedure was freezing the scar tissue from within in a single session. The results were satisfying. The keloids showed a decrease of redness and hardness. Also subjective symptoms as thickness or itching were reduced. Every parameter was assessed on a scale of 0-3. Every change was statistically significant. The most common adverse effect was hypopigmentation of the skin. The time of observation was relatively long - 18 months. No additional side effects and recurrence were observed during these 18 months. After the procedure there was mild local swelling and epidermolysis. What is more, in histopathology examination, the collagen fibers were more ordered. The observed changes were vascular damage, cellular necrosis and collagen degeneration. The authors suggested this method of cryotherapy as better and safer than cryotherapy by using contact or spray probes.

The usage of intralesional cryotherapy for the treatment of 27 patients with 29 keloid scars, during 1 year observation observed the keloids in each of the Fitzpatrick skin types (van Leeuwen, van der Wal, et al., 2015). The researchers did not investigate the hypertrophic scars. There were noticed an average 63% decrease of keloid scars which was statistically significant. The recurrence was observed in 7 keloids. Every patient after the procedure had hypopigmentation but the rate then subsided into 69%. In 9 cases the hypopigmentation was permanent. The scar elasticity improved in 57% of treated keloids. Notwithstanding, it deteriorated in 50% of recurring scars. Patients showed a 52% improvement compared with baseline (statistically significant). The authors paid attention to different numbers of side effects and effectiveness of therapy in different groups of Fitzpatrick skin type patients. The types from III to VI had more incidents of persistent hypopigmentation. Additionally, for those patients this side effect was especially problematic from a psychological point of view. Also, the recurrence of keloid was observed in 6/7 patients when type of skin was over III. The conclusion of authors suggest that this type of keloid treatment can be useful therapy, but not always effective. Moreover, Non-Caucasian patients had higher risk of side effects and it was suggested that they should not be treated by this therapy.

Another review of 8 different studies about intralesional cryotherapy in keloid scars treatment established the average decrease of volumes of scars from 51 to 63% (van Leeuwen, Bulstra, et al., 2015). What's important, there was no complete resolution of the keloid. Recurrence occurred in up to 24% of cases. However, this therapy was assessed as an useful option in non-surgical treatment of keloids. The authors paid attention to the problem of hypopigmentation in some groups of patients (type III-VI in Fitzpatrick type skin)

as a side effect. Nonetheless, they confirmed intralesional cryotherapy as an effective and minimal invasive option of keloid treatment.

The review of 15 articles about intralesional cryotherapy showed that this treatment can lead to reducing keloid scars and subjective symptoms (O'Boyle et al., 2017). There were only a few side effects reported, mainly hypopigmentation, pain during injection and recurrence of keloids. There were a few complete reductions. The authors paid attention to the need for more research to determine the place of this therapy in treatment of keloids as it could become an effective option.

An examination of using argon gas-based systems in cryotherapy treatment of keloids showed satisfactory results (van Leeuwen et al., 2014). The volume of keloid tissue decreased about 62%. The rate of reduction was dependent on Fitzpatrick skin type - 48% in group I-III and 66% in group IV-VI. The keloids previously treated NO were decreased about 38%. 5 keloids were recurrence and 4/5 belong to grup IV-VI of Fitzpatrick skin type. Moreover, the treatment led to decreased symptoms of itching and pain. The authors indicated that this therapy was accurate and controlled in freezing of keloid tissue. However, the patients with dark skin were more vulnerable to side effects such as hypopigmentation. Also, the authors advised against using this therapy in previous treatment by cryotherapy groups of patients.

The study in vitro was conducted to prove the beneficial effect of cryotherapy in keloids treatment (Dalkowski et al., 2003). The cell cultures obtained from 13 different keloids and from 10 healthy skin specimens as a control group were frozen and then investigated in case of proliferation, viability, synthetic activity and differentiation of dermal fibroblasts. The results showed significant reduction of the fibroblasts activity and decreased collagen production in comparison to the control group. The study was concluded as the cryotherapy directly modifies keloid fibroblast function. The findings confirm the clinical effectiveness of intralesional cryotherapy. Additionally it shows that the mechanism is not only destruction of overgrown tissue but at the same time modifying the function of fibroblasts.

Results

The analysed 28 studies - 6 about laser treatment containing around 450 patients and 500 scars; 11 about silicone gel treatment containing around 1200 patients and 1350 scars; 5 about 5-fluorouracil treatment containing around 210 patients and 220 scars and 6 about intralesional cryotherapy treatment containing around 180 patients and 190 scars; (some studies did not specified those data) can be concluded in the following results.

In case of laser therapy the reduction of size, thickness and redness was observed. Additionally vascularity, or symptoms such as pain and pruritus has improved. The method also showed limited adverse effects and was summed up as a safe one.

The usage of silicone gel in keloid scars therapy demonstrated some clinical benefits in terms of prevention and treatment. Again the reduction of volume, redness and general appearance was observed. Additionally there was reported relief from symptoms such as pruritus, pain or discomfort. It was a well-tolerated and non-invasive way. Only the long-term effects and rate of recurrence was not examined.

Another effective treatment seems to be the injections of 5-fluorouracil. Both scar appearance as well as symptoms showed improvement. What is important, the in vitro studies showed the cellular mechanisms and histopathological evidence to confirm the general clinical findings. The side effects were generally mild and not significant for patients.

In case of intralesional cryotherapy the significant reduction of the keloid scars was observed. It was also followed up by reduction of symptoms including pain, stiffness or pruritus. One more time, some research confirms the clinical results by some histopathological procedures. The results seemed to be the most effective ones, when it comes to some cases of total reduction of the keloids observer. Nonetheless, it has to be underlined that the adverse effect of hypopigmentation was commonly observed.

Discussion

Laser treatment

After analysis of 6 different studies of laser treatment of keloid scars, it can be concluded that the therapy may be effective and have potential benefits. The healing process was successful and in general did not bring any serious side effects. Different lasers reduced the sizes of scars as well as the thickness, redness or itching problems. Patients were satisfied with the process. However, all of the studies analysed, even the metaanalysis, were based on very small groups of patients, usually also very specified ones by type of skin, age or even gender. The researchers were also often limited to particular body areas and did not spread used protocols to the whole body, which can be problematic due to different thickness or elasticity of the skin according to its location. Additionally, the studies, even if the follow-up was conducted, represented a very short time of long lasting effects. The medical knowledge clearly shows that keloids may regrow after healing and in some cases they may appear even more spread or thick. It needs to be underlined that patients were in general satisfied with the research participation and their compliance was high due to results of treatments. However the studies cannot be relevant to draw any medical relevant conclusions due to limitations of particular studies which were regularly repeated in almost every study.

Silicone treatment

The literature of 11 different articles including reviews and metaanalysis of silicone gel treatment in keloid scars healing process clearly demonstrates that this way may be very effective. It is also confirmed that it is a very popular, noninvasive and safe way of treatment. Although, the evidence is not strong enough to become a golden-standard in medicine. The studies consequently report improvements in the thickness, redness and pruritus of keloid scars after using silicone treatment. It is suggested that the mechanism is rather hydration of the stratum corneum, reduction of transepidermal water loss, modulation of fibroblast activity, and possibly mast cell regulation. It could be suggested that there should be some randomised studies conducted to assess the method by comparing to different mechanisms of treatment. Some meta-analysis investigated in the study confirm consistently that the scar appearance and symptoms are improved compared to no treatment. However, the most common limitations in the literature are lack of randomization, small groups of patients, no long-term efficacy or high risk of bias. Due to those, the rate of certainty of evidence results to be low to even very low. It was also confirmed that silicone gel has great effects in treatment of hypertrophic scars. However, it may be insufficient for aggressive or recurrent keloids.

5-fluorouracil

The collected literature shows that 5-fluorouracil can be useful in keloid scars treatment. In most studies it significantly reduced the sizes, redness and thickness of keloids. Additionally, the therapy statistically showed no significant side effects. What is important, this method of treatment was successfully researched histopathologically. The results also confirmed the effectiveness and reduction of fibroblast density and collagen deposition. Simultaneously, the experts in another study investigated the cellular mechanisms and showed the arrest of G2 cell cycle and induction of apoptosis in keloid fibroblasts. Nonetheless, those studies were conducted in vitro and should be followed up by some research on human patients. Nevertheless, it should be underlined that 5-fluorouracil was the method investigated in more scientific ways than just confirmed by observation of patients clinically. Even if some of the mechanisms of treatment's work were examined, it should be notified that 5-fluorouracil showed some recurrence ratio. The longest research lasted a year, which is at the same time too long to be named a long-lasting research and still longer than other investigated studies of all the methods. The other limitations are small groups of patients, lack of standardized treatment protocols or some inconsistent outcome measures.

Cryotherapy

Cryotherapy seems to be one of the best investigated methods of treatment from the ones described in this article. It is common that the liquid nitrogen applied externally has plenty of side effects such as hypopigmentation, blistering or infection. Additionally, in case of larger keloids, multiple sessions of cryotherapy are required. In this examination we decided to check the results of intralesional cryotherapy, which is a novel treatment for keloid scars in which the scar is frozen from inside. The results show that the method results in creating new scars with no keloidal characteristics. The reactions such as inflammation are reduced and the hypopigmentation ratio is significantly lower in intralesional cryotherapy than in standard external methods. It is also confirmed that due to complex mechanisms of work, the recurrence rate is lower than in other methods. The modification of fibroblast activity is researched in vitro which just confirms the clinical results and the evidence of cellular necrosis. Nonetheless, it has to be underlined that this way of treatment results in the highest risk of side effects in terms of hypopigmentation. However, the rate of

effectiveness seems to be higher than in different methods as well. The cryotherapy treatment still needs some more standardized protocols and measures. The time of long-term effects and the recurrence rate should also be confirmed, even if this way of treatment showed the longest observations from the researched methods.

Conclusions

Collectively, it can be suggested that laser therapy may play a valuable role in keloid treatment but it has to be considered whether it is the main or only supportive role. Further research is still needed with well standardized and randomized groups of patients and follow-up long term results. Similar conclusions may be drawn from the silicone gel treatment. This way seems to be very effective especially in the primary stages of treatment. However, further research in particular in long-term effects should be studied by conducting well-designed randomized and standardized trials. It is necessary to make the results clinically meaningful. In case of 5-fluorouracil the most important part which needs further investigation in some studies on groups of patients controlling the antifibroblastic and pro-apoptotic effects. The treatment seems to be a safe and effective option. The therapy may be valuable in steroid-resistant keloids and in the sensitive areas. Nonetheless, the rate of recurrence is needed to be examined in long-term studies. The very promising and valuable way of keloid treatments seems to be intralesional cryotherapy. The studies confirm its effectiveness and safeness. What is more, the results are confirmed histopathologically and by some in vitro research. The way of treatment looks particularly suitable for bulky or refractory keloids. The only found disadvantages are pain during the procedure and relatively high rate of hypopigmentation of the skin especially for darker skin shades.

Even if examined methods of treatment showed some effectiveness there is no sufficient evidence that a single one of them could become a monotherapy of keloid scars. There are plenty of limitations of the studies and accordingly lack of medical based knowledge. The methods cannot be standardized and compared. It could be suggested that monotherapy may not be a good way of keloid scars treatment. Possibly, there is needed research on comparing combined therapies. Nonetheless, the studies have to be on big randomized groups of patients and it is required to confirm the follow-up studies to examine long-term effects and the rate of recurrence of keloids. In this point it can be only concluded that the intralesional cryotherapy, despite its side effects, seems to be the most promising option but cannot be qualified as a golden standard of keloid scars monotherapy. The final conclusion is that there is a need for examination of some combined therapies of keloid scars to create the most effective schema of scar-modulating therapy.

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